REMARKS

I. Introduction

In response to the Office Action dated February 4, 2008, claims 14 and 25 have been amended. Claims 14, 15, 19, 25 and 26 remain in the application. Re-examination and re-consideration of the application, as amended, is requested.

II. Claim Amendments

Applicants' Attorney has amended claims 14 and 25 as indicated above. These amendments are fully supported by the specification as filed and introduce no new matter. Specification support for embodiments of the invention where the compound of the formula (I) comprises an R_1 moiety that is a hydrogen or a lower alkyl group is found for example at paragraphs 16 to 18 of the present application.

Paragraph 16 of the present application teaches for example general compounds of formula I (i.e. which include the group R1, as recited in paragraph 11 of the present application) and further identifies a number of prior art documents that disclose illustrative compounds of formula (I) where R_1 is hydrogen or lower alkyl group (see, e.g. U.S. Patent Nos. 4,582,916, 6,420,369, 6,559,293, 6,583,172, and EP-B-0, 138,441 which were incorporated by reference). Paragraph 16 in the specification also specifically teaches a number of compounds where R_1 is hydrogen or a lower alkyl methyl group. In this context, paragraphs 17 and 18 then discuss topiramate in detail (as well as functional analogues of topiramate), a compound of formula (I) where R_1 is hydrogen.

For the reasons noted above, one of skill in the art would agree that the descriptions in the specification of compounds having formula (I) where R_1 is hydrogen or a lower alkyl group reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, clearly possessed compounds having formula (I) where R_1 is hydrogen or a lower alkyl group. Consequently, the amendment to claim 14 is fully supported by the specification as filed and introduces no new matter.

III. Claim Objections

On page (3) of the Office Action, claim 14 was objected to due an absence of a definition for R_1. Claim 14 has been amended hereinabove to overcome this rejection.

On page (3) of the Office Action, claims 25 and 26 were objected to due to improper dependencies. Claim 25 has been amended hereinabove to overcome this rejection.

IV. Prior Art Rejections

On page (3) of the Office Action, claims 14 and 15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Dursun et al. (Canadian Journal of Psychiatry, 2000) and http://www.answers.com/topic/dyskenesia. On page (5) of the Office Action, claims 19, 25 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Dursun in view of Wolters et al., CMAJ, 1989 (Wolters).

Applicants respectfully traverse these rejections because for example, one of skill in the art would not agree with the Patent Office's belief that the myoclonic jerks observed to arise from the administration of clozapine are a type of dyskinesia. One of skill in the art would instead note that the art in this area of medicine teaches that myoclonic jerks (myoclonus) comprise a pathological syndrome that is distinct from dyskinesias (i.e. chorea, athetosis, dystonia) in terms of: (1) clinical manifestations (phenomenology); (2) underlying brain mechanisms and; importantly (3) response to pharmacological intervention. For these reasons, it would not have been obvious to one of ordinary skill in the art at the time of the invention to have considered the myoclonic jerks observed to arise from the administration of clozapine, as a type of dyskinesia.

A possible reason for the Patent Office's incorrect characterizations of dyskinesias and myoclonic jerks is their reliance on a website known as www.answers.com. In this context, Applicants' Attorney respectfully points out that this website is not considered to be an authoritative source of technical information by those of skill in this art. In addition, the Patent Office further fails to provide evidence that the definition provided on this website would even have been available at the priority date of the above application or that it would have reflected the art at that time the application was filed. Consequently, the Patent Office's reliance on the technical characterization of dyskinesias (i.e. what they encompass and how they are distinguished from other movement disorders) as provided on an "answers.com" website is misplaced. Applicants detailed arguments in this regard are provided below.

Those of skill in this art understand that the term "dyskinesia" (from the Greek) literally means "abnormal movement". As shown by the Patent Office's interpretation of the information

provided on an "answers.com" website, this term could potentially, therefore, be used to describe any form of disordered movement (e.g. tripping over a log and falling down). However, those of skill in this art understand that the pathological syndrome known to artisans as dyskinesia does not encompass all types of abnormal movements and instead is characterized by a very specific constellation of pathological features. For example, the term "dyskinesia" is never used to describe the involuntary movements and muscle contractions that accompany convulsive or epileptic disorders (fits). Instead, the term dyskinesia is used to describe abnormal movements that have a squirming or writhing character (often also called chorea, athetosis or dystonia). This is shown for example by the teaching in Applicants' specification, which provides a definition of dyskinesias in paragraphs 2, 3, 5 and 13 (e.g. paragraph 3: "Such disorders can occur as a consequence of inherited or acquired disease, idiopathic neurodegeneration or they may be iatrogenic. The spectrum of disorders is very diverse, ranging from those associated with poverty of movement (akinesia, hypokinesia, bradykinesia) and hypertonia (e.g. Parkinson's disease, some forms of dystonia) to the involuntary movement disorders (hyperkinesias or dyskinesias e.g. Huntington's disease, levodopa-induced dyskinesia, ballism, and some forms of dystonia.)". Applicants' proper definition of dyskinesia in their specification is confirmed by the definition of dyskinesias provided on the Parkinson's disease website (www.parkinson.org) as discussed in the Amendment dated June 4, 2008 (i.e. as abnormal, involuntary movements of the voluntary muscles, e.g. in the arm, leg, hand, etc. Such involuntary movements can vary greatly in pattern from barely discernible twitches and jerks to twisting, writhing movements involving almost the entire body).

Contrary to the Patent Office's assertion in the outstanding rejection under 35 U.S.C. 103(a), myoclonic jerks (myoclonus) comprise a pathological syndrome that is distinct from dyskinesias (i.e. chorea, athetosis, dystonia) in terms of clinical manifestation (phenomenology), underlying brain mechanisms **and, importantly, response to pharmacological intervention**. For example, regarding clinical manifestation (phenomenology), myoclonic jerks are very rapid, electric-shock-like twitches of muscles caused by paroxysmal activity in the motor neurons that control them. They are usually regarded as akin to convulsive or epileptic activity which, as discussed above, is never described as a dyskinesia. In contrast, dyskinesias are associated with writhing movements (often called chorea or athetosis). Regarding brain mechanisms, myoclonic jerks are caused by uncontrolled excitation of the motor cortex and/or motor neurons that control muscles. They often

occur following acute insult or injury to the cerebral hemisphere, or brain stem, by trauma, surgery or stroke, situations which also commonly lead to convulsive or epileptic activity (and to which myoclonic jerks are considered to be akin). Dyskinesias, on the other hand, are caused by dysfunction of quite different parts of the nervous system, called the basal ganglia, and they are usually the consequence of chronic neurodegenerative conditions. Regarding pharmacological intervention, myoclonic jerks are usually treated with anticonvulsant drugs or sedatives that calm or inhibit the paroxysmal discharge of neurons. **Dyskinesias, on the other hand, are very difficult to treat and are never treated with anticonvulsants. There are currently no drugs approved by the FDA for the treatment of dyskinesias.**

In view of the above-noted well known differences between myoclonic jerks and dyskinesia, the skilled person would not agree with the Patent Office's determination that myoclonic jerks are a type of dyskinesia. Consequently, an artisan familiar with the disclosure in Dursun et al. (which provides teaching in relation to myoclonic jerks only), would not agree that this disclosure can be used to envision new therapeutic regimens for the treatment of dyskinesias. Illustrating this, the disclosure in Dursun et al. fails to teach or suggest that an anticonvulsant such as a compound of formula I as defined in claim 14 (including topiramate) would have been useful for treating dyskinesias. For these reasons, the disclosure in Dursun et al. cannot be combined with the disclosure in "answers.com" website cited by the Patent Office in a way that teaches or suggests the claimed invention. For this reason, Applicants respectfully request a withdrawal of the rejection to claim 14 under 35 U.S.C. §103(a).

The Patent Office further cites Wolters et al. in combination with Dursun et al. in respect to claims 19, 25 and 26. These claims are dependent upon claim 14, which we understand is considered by the Examiner to be non-obvious over the disclosures of Dursun et al. and Wolters et al. in combination. The Examiner should consider claims 19, 25 and 26 also to be non-obvious over the disclosures of these documents by virtue of their dependency on claim 14. In particular, Wolters cannot remedy the deficiencies of the Dursun disclosure because it too fails to provide any teaching to use an anticonvulsant such as a compound of formula I as defined in claim 14 (including topiramate) for treating dyskinesias. Instead, Wolters et al. discusses the treatment of Parkinson's disease and teaches that treatment with Levodopa may cause adverse reactions such as dyskinesia (see the section entitled "Dopamine Precursors" on pages 508 and 509 of Wolters et al.). The only

teaching in Wolters et al. as to how such adverse reactions may be alleviated is provided in the seventh paragraph on page 511 of Wolters et al. where it is suggested that this may be achieved by altering the daily dose of Levodopa. There is no teaching or suggestion in Wolters et al. to use another agent to treat dyskinesia, let alone any suggestion as to what agent this might be, much less any teaching or suggestion in Wolters et al. to use an anticonvulsant such as a compound of formula I as defined in claim 14 (including topiramate) for treating dyskinesias. Thus, neither Dursun et al. nor Wolters et al. provides any teaching that would have led, or even motivated, the skilled person to use a compound of formula I such as topiramate for treating dyskinesias. Thus, the subject matter of claims 14, 15, 19, 25 and 26 is non-obvious over the disclosures of these documents in combination. For this additional reason, Applicants respectfully request a withdrawal of the rejection under 35 U.S.C. §103(a).

In addition, one of skill in the art further understands that schizophrenia (as disclosed in Dursun) and Parkinson's disease (as disclosed in Wolters) are very different pathological conditions that result from different underlying physiological mechanisms in the brain. For example as noted in the Wolters disclosure, Parkinson's disease is a pathological condition characterized by decreased dopaminergic activity in the brain (see, e.g. Wolters et al., the paragraph bridging pages 507-508). In contrast, those of skill in the art understand that schizophrenia is a pathological condition characterized by increased dopaminergic activity in the brain (see, e.g. the abstract of Rao et al., Eur Arch Psychiatry Neurol Sci. 1984; 234(1): 8-12, a copy of which was provided with the Amendment dated June 4, 2008). For this reason, the artisan concurrently understands that the clinical regime for the treatment of dyskinesias which arise as a side-effect of a therapeutic agent, requires a distinct clinical regime from the clinical regime required for the treatment of schizophrenics exhibiting myoclonic jerks caused by clozapine (as disclosed in Dursun).

Because of, for example, the very different dopaminergic activity profiles that are observed to occur in the brain in individuals suffering from Parkinson's disease as compared to those suffering from schizophrenia, one of skill in the art would further disagree with the Patent Office's belief that artisans are motivated to mix and match therapeutic agents in these different pathologies such that "it would have been obvious to one of ordinary skill in the art at the time of the invention to have employed topiramate to treat the dyskinesia-like side effects caused by L-DOPA as taught by Wolters" (Office Action page 6). Instead, in view of the "opposite" dopaminergic brain profiles

known to characterize these two pathological conditions, one of skill in the art would more likely believe that an agent observed to be useful to treat a patient suffering from Schizophrenia (i.e. having an increased dopaminergic activity in the brain) would be unsuitable for a patient with Parkinson's disease (i.e. having an decreased dopaminergic activity in the brain). In fact, because Schizophrenia and Parkinson's disease a exhibit these "opposite" profiles of dopaminergic activities in the brain, the artisan familiar with this difference between these pathological conditions is taught away from combining the Dursun and Wolters disclosures.

A reference's disclosure teaches away if a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference. *In re Gurley*, 27 F.3d 551, 553, 31 U.S.P.Q.2d 1130 (Fed. Cir. 1994). As noted in M.P.E.P. 2145(X)(D)(2), references cannot be combined where reference teaches away from their combination. In this context, because skilled artisans are aware that Schizophrenia and Parkinson's disease exhibit "opposite" profiles of dopaminergic activities in the brain, one of skill in the art would be would be discouraged from mixing and matching therapeutic agents used to treat schizophrenia with agents used to treat Parkinson's disease. For this additional reason, one of skill in the art cannot combine the disclosure in Dursun with the disclosure in Wolters to arrive at the invention recited in claim 14. For this additional reason, Applicants respectfully request a withdrawal of the rejections under 35 U.S.C. §103(a).

In addition, the various elements of Applicants' claimed invention together provide operational advantages over Dursun and Wolters. In addition, Applicants' invention solves problems not recognized by Dursun and Wolters. Thus, Applicants submit that independent claim 14 is allowable over Dursun and Wolters. Further, the dependent claims are submitted to be allowable over Dursun and Wolters in the same manner, because they are dependent on the independent claims, and thus contain all the limitations of the independent claims. In addition, the dependent claims recite additional novel elements not shown by Dursun and Wolters.

V. Conclusion

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that

can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

GATES & COOPER LLP
Attorneys for Applicant(s)

Howard Hughes Center
6701 Center Drive West, Suite 1050
Los Angeles, California 90045
(310) 641-8797

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By: /William J. Wood/
Name: William J. Wood
Reg. No.: 42,236

WJW/bjs

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